REMARKS

Currently, claims 27, 28, 44, 45, 48, 50-56 and 59-69 are rejected. Claims 46, 47, 57 and 58 are allowed, and claim 49 is objected to. Following entry of the present Amendment, claims 27, 44, 48 and 63 are amended, and claims 53 - 56 and 66 - 67 are cancelled. It is believed no new matter has been added. Applicants reserve the right to file continuation applications based on claim scope that may have been narrowed due to amendments, and to cancelled claims.

The Examiner indicates on page 13 of the Office Action that claims "45-47 and 57-58 are allowed." In view of the other portions of the Office Action, and item 5 of the Office Action Summary Sheet (claims 46, 47, 57 and 58 is/are allowed), Applicants assume claim 45 is not allowed in the Office Action, and claims 46, 47, 57 and 58 are allowed.

As indicated in item 7 of the Office Action Summary Sheet, claim 49 is objected to; however, no further discussion of claim 49 is provided in the Office Action.

Applicants respectfully request the Examiner clarify the nature of the objection of claim 49, and confirm claim 45 was not allowed.

I. 35 USC § 103(a) rejection

Claims 27, 59, 63, 64 and 65 are rejected under 35 USC § 103(a) as being unpatentable over US Patent 5,256,766 (Coughlin) in view of US Patent 5,352,664 (Carney). Applicants respectfully traverse the rejection and request it be withdrawn. Coughlin discloses a thrombin receptor, and Carney discloses purification of thrombin receptors. However, Coughlin and Carney (either alone, or in combination) fail to disclose or suggest the claimed invention.

In contrast to Coughlin and Carney, the instant claims are directed to isolated C140 receptor polypeptides, not thrombin receptor fragments. Claim 27 is directed to an isolated C140 receptor polypeptide having at least 15 consecutive amino acids encoded by a nucleic acid molecule which hybridizes under stringent conditions a nucleic acid molecule complimentary to SEQ ID NOs 3 or 62. The stringent conditions are set forth in the text of the claim. Claim 63 is

directed to an isolated polypeptide comprising a fragment of a C140 receptor polypeptide at least 10 consecutive amino acids in length.

The Examiner has identified a 10 consecutive amino acid stretch (LNITTCHDVL) in Coughlin's thrombin receptor which is present in SEQ ID NOs 3 and 62. According to the Examiner, "[t]he nucleic acid encoding the LNITTCHDVL sequence and flanking sequences are sufficient to encode a 15 consecutive amino acid sequence that is approximately 80% homologous to the corresponding nucleotide sequences of SEQ ID NO:3 or 62. It must be assumed, absent evidence to the contrary, that the sequence encoding the thrombin polypeptides would be capable of hybridizing, under the stringency conditions recited in the claims, to the nucleic acids complementary to SEQ ID NO:3 or 62." Office Action, page 3. Applicants assume that Coughlin does not actually disclose such a 15 consecutive amino acid sequence, but rather discloses longer sequences comprising such a sequence. Carney teaches the purification of thrombin receptors. The Examiner finds that one of skill in the art would be motivated combine the references, to express the protein taught in Coughlin, and isolated the protein as taught by Carney, because it would be necessary step in the production of antibodies to the protein of taught by Coughlin. Given the teachings of the prior art, a skilled artisan would have a reasonable expectation of success in practicing the claimed invention.

Applicants respectfully submit that the Examiner has not established a *prima facie* case of obviousness. To establish a prima facie case of obviousness, there must be suggestion or motivation to modify the reference, or to combine the references. Second, there must be a reasonable expectation of success. Finally, the prior art reference must teach or suggest all the claim limitations.

A. Coughlin and Carney do not suggest isolation of any 10 amino acid peptide, or 15 amino acid peptide and nucleic acid sequence encoding it.

The Examiner states Coughlin "contains a 10 consecutive amino acid stretch (LNITTCHVDL) in common with the C140 receptor polypeptide. . . [T]he nucleic acid encoding the LNITTCHDVL sequence and flanking sequences are sufficient to encode a 15 consecutive amino acid sequence that is approximately 80% homologous to the corresponding nucleotide sequences of SEQ ID NO:3 or 62." Office Action, page 3.

Coughlin and Carney fail to teach or suggest isolation of the LNITTCHDVL amino acid stretch (with or without the 5 flanking amino acids). Carney teaches the purification of thrombin peptides which bind to the thrombin receptor, and purification of the entire thrombin receptor; however, Carney fails to disclose purification of any fragment or portion of the thrombin receptor, or C140 receptor at least 10 or 15 consecutive amino acids in length. The closest that Coughlin comes to identification of the 10 amino acids LNITTCHDVL (with or without the 5 flanking amino acids) is at col. 11, lines 27-40, whereby a 26 amino acid peptide (KEQTIQVPGLNITTCHDVLNETLLEG) is used as an immunogen to prepare antibodies. The hypothetical 15 amino acid peptide referred to by the Examiner is not disclosed in these references, nor is any nucleic acid sequence encoding it disclosed.

If the 26 amino acid peptide disclosed in Coughlin is aligned with the corresponding amino acid sequence of SEQ ID NOs 3 and 62, it can be seen that the sequences only contain 69% amino acid identity (16 out of 26 amino acids). With respect to claim 27, if the 78 nucleotides of Coughlin (encoding the corresponding 26 amino acids) are aligned to the Applicants' nucleotide sequence, there is only 63% homology between the two sequences (49 out of 78 nucleic acids). The Examiner has provided no evidence this 78 nucleic acid molecule of Coughlin will hybridize to a nucleic acid complementary to either of SEQ ID NOs 3 or 62 under stringent conditions given that there is only 63% homology/complementary between the sequences.

B. Coughlin teaches away from isolation of any hypothetical 10 amino acid peptide, or 15 amino acid peptide and nucleic acid sequence encoding it.

Coughlin actually teaches away from isolating the LNITTHDVL sequence (with or without 5 amino acid flanking sequences), and/or fails to teach modifying the 26 amino acid peptide (KEQTIQVPGLNITTCHDVLNETLLEG) to produce the LNITTHDVL sequence (with or without the 5 amino acid flanking sequences). A modification to the 26 amino acid peptide to the hypothetical 10 amino acid peptide (with or without 5 flanking amino acids) renders the 26 amino acid peptide unsatisfactory for its intended purpose, that is, to prepare desired antibodies to the thrombin receptor. Coughlin provides general statements as to the desirability of using portions of the thrombin receptor, however provides no disclosure or suggestion that the 10

amino acid (with or without 5 flanking amino acids) can function as an immunogen to produce antibodies to the thrombin receptor, or even the C140 receptor. There are no reasons in Coughlin suggesting or disclosing that the 10 amino acid stretch alone or in combination with 5 flanking amino acids would be suitable for the production of antibodies against the thrombin receptor or C140 receptor. "If proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification." *In re Gordon*, 733 F.2d 900 (Fed. Cir. 1984). There simply is no motivation or suggestion to combine or modify the references, and there is no reasonable expectation of success. One of skill in the art would not be motivated to isolate the 10 amino acid (with or without the 5 flanking amino acids) to produce antibodies to the thrombin or C140 receptor, much less isolate a 15 amino acid polypeptide encoded by a nucleic acid which hybridizes to a sequence complementary to SEQ ID NOs 3 or 62 under stringent conditions.

C. Even if the hypothetical 15 amino acid peptide described by the Examiner were derivable from Coughlin and Carney, the nucleic acid sequence encoding it would not meet the limitations of the claims.

The Examiner states Coughlin "the nucleic acid encoding the LNITTCHDVL sequence and flanking sequences are sufficient to encode a 15 consecutive amino acid sequence that is approximately 80% homologous to the corresponding nucleotide sequences of SEQ ID NO:3 or 62."[1] Office Action, page 3. The Applicants fail to see how this *nucleotide sequence* (not specifically disclosed in Coughlin) encoding the 15 consecutive amino acid sequence is approximately 80% homologous with the corresponding *nucleotide sequence* of SEQ ID NOs 3 or 62. Depending on how the 5 flanking amino acids are broken up (i.e., 2 before and 3 after the LNITTCHVDL sequence, or 5 before and 0 after), the homology between Coughlin and a nucleotide complementary to SEQ ID NOs 3 or 62 is at most 71% (i.e., 5 amino acids before and 0 after the LNITTCHDVL sequence), or at least 69% (i.e., 0 before and 5 after the

[1] The Applicants have attempted to read the statement as meaning that the 15 *amino acid* sequence (which is not disclosed in Coughlin) is 80% homologous with the corresponding 15 *amino acid* sequence of SEQ ID NOs 3 and 62. However, the particular amino acids encoded by 2 nucleotide sequences does not determine the hybridization between those 2 nucleotide sequences. Rather, hybridization between the 2 nucleotide sequences is determined by the homology between the nucleotide sequences and hybridization conditions.

LNITTCHDVL sequence). It is difficult to see how the 45 nucleic acid molecule derived from the complete sequence of thrombin receptor of Coughlin (encoding a 15 amino acid sequence) can hybridize to a nucleic acid molecule complementary to SEQ ID NOs 3 or 62 under stringent conditions if the nucleic acids are, at most, 71% homologous/complementary.

In arguendo, even if: 1) the LNITTCHDVL sequence with 5 flanking amino acids is disclosed by Coughlin; 2) Carney teaches the purification of portions of the thrombin receptor and 3) there were motivation to combine the teachings of Coughlin and Carney, the combination of Coughlin and Carney still fails to disclose all the limitations of the claimed invention. The Examiner stated, "[i]t must be assumed, absent evidence to the contrary, that the sequence encoding the thrombin polypeptides would be capable of hybridizing, under the stringency conditions recited in the claims, to the nucleic acids complementary to SEQ ID NO:3 or 62." Office Action, page 3. Applicants respectfully submit this statement lacks support in the instant application or any of the references cited. The Examiner is basing the rejection on inherent properties of the amino acid stretch; particularly, the nucleic acid encoding the 10 amino acid stretch and flanking sequences is inherently capable of hybridizing to a DNA molecule complementary to SEQ ID NO 3 or 62 under stringent conditions. Without support or evidence, it cannot be said that the nucleic acid sequence encoding the 10 amino acid and flanking amino acids disclosed in Coughlin is capable of hybridizing to a nucleic acid complementary to SEQ ID NOs 3 or 62 under the stringent conditions described. The Examiner is burdened with disclosing the basis of the assumption.

Neither Coughlin or Carney, alone or in combination, suggest that any of the polypeptides disclosed by Coughlin are C140 receptor fragments, or C140 receptor polypeptides at least 15 consecutive amino acids encoded by a nucleic acid molecule which hybridizes to a nucleic acid molecule complimentary to SEQ ID NO:3, or SEQ ID NO:62 under stringent conditions, much less identify the stringent conditions as specified in the instant claims. *A fortiori*, with respect to claim 27, the references cannot disclose that the C140 receptor polypeptide is encoded by a nucleic acid molecule which hybridizes under stringent conditions to a nucleic molecule complementary to SEQ ID NOs 3 or 62, especially because neither Coughlin or Carney disclose or suggest those stringent conditions.

As Coughlin and Carney fail to disclose the limitations of claim 27 and 63, they also fail to disclose all of the limitations of the claims dependent there from. Accordingly, Applicants respectfully request that the rejection be withdrawn.

II. 35 USC § 112, first paragraph rejections - Enablement

Claims 27, 28, 44, 45, 50 and 51 are rejected under 35 USC § 112, first paragraph, as failing to comply with the enablement requirement. Specifically the specification as originally filed does not provide enablement for any isolated polypeptide having at least 15 consecutive amino acids encoded by a nucleotide sequence capable of hybridizing under stringent conditions to the complement of SEQ ID NO:3 or 62, or a polypeptide having at least 75%, 90%, or 95% amino acid sequence identity to either of SEQ ID NO:4 or 63. Claims 27 and 44 (from which claims 28, 45, 50 and 51 depend) have been amended to recite an "isolated C140 receptor polypeptide". In view of the amendments to the claims, Applicants respectfully traverse the rejection, and request the rejection be withdrawn.

With regard to claim 27 (from which claims 28, 50 and 51 depend), Applicants submit that the claims as amended are enabled. The specification identifies C140 receptor polypeptide sequence, as well as several nucleic acid sequences encoding it. A person of skill in the art would be well able to predict the amino acid sequence encoded by a nucleic acid, thus would be easily be able to identify whether a nucleic acid sequence encodes at least 10 consecutive amino acids of the C140 receptor polypeptide. DNA hybridization techniques are well known in the art, and a person of skill in the art would be easily able to determine whether a nucleic acid can hybridize to the complementary sequence of SEQ ID NOs 3 and 62. One of skill in the art merely needs to perform a simple experiment to determine whether a nucleic acid sequence hybridizes to a nucleic acid molecule complementary to SEQ ID NOs 3 and 62. The present specification contains an exact description of specific characteristics that distinguish the characteristics of polypeptides, that is, they must be encoded by nucleic acids having specific properties. The structural limitations of hybridization to defined sequences is by itself sufficient to enable one of skill in the art to practice the claimed invention.

Applicants assert that it would be routine and well within the skill of one in the art to determine whether an isolated C140 receptor polypeptide is encoded by a nucleic acid which hybridizes to the nucleic acid molecule complementary to SEQ IDs 3 or 62 by simple experimentation known by those in the art. Applicants' nucleic acid sequences are defined and specifically provided as SEQ ID NOs 3 and 62. The specification teaches how to isolate such nucleic acid sequences, and nucleic acids can be synthesized in any number of methods known by those of skill in the art. Given the detailed structural characterization of the C140 receptor from mice and human, the disclosure that the Applicants have provided in the specification provides ample description to permit of skill in the art to appreciate and understand the claimed invention and to identify an isolate C140 polypeptide that may fall within the limitations of the claims.

Applicants also submit that claims 28, 44, 45, 50 and 51 as amended are enabled. The identity of SEQ ID NOs 4 and 63 are disclosed. Amino acids are known in the art, and it is clearly within the skill of one of skill in the art to determine the percent identity of an amino acid sequence with SEQ ID NOs 4 and 63 by lining up the amino acid sequences. At page 12, lines 11 - 20 of the specification as filed, the Applicants provide guidance as to how to determine percent identity.

The fact that *some* experimentation may be required is irrelevant; what is relevant is whether *undue* experimentation is required. Enablement "is not precluded even if some experimentation is necessary, although the amount of experimentation needed must not be unduly extensive." *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367 (Fed. Cir. 1986). The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. MPEP § 2164.01, 8th ed., rev. 4.; *In re Certain Limited-Charge Cell Culture Microcarriers*, 221 USPQ 1165, 1175 (Int'l Trade Comm'n 1983).

In support of the nonenablement rejection, the Examiner has referred to the factors set forth in *In re Wands*, 858 F.2d 731 (Fed.Cir. 1988). In that case, the Court of Appeals for the Federal Circuit reversed the Patent Office's finding of nonenablement and identified a variety of factors which may be relevant to whether practicing a claimed invention would require undue experimentation: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the

invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. As the *Wands* Court held, whether undue experimentation is required is not a single, simple factual determination, and no one factor is necessarily determinative. Rather, enablement or lack of enablement is determined by weighing all of the applicable factual considerations. Applying the *Wands* factors to the instant case, it is clear that practicing the instant invention would not require *undue* experimentation.

In this case (1) the quantity of experimentation is low because (2) the amount of direction or guidance presented in the application and prior art is high, (3) the presence of working examples is not required because those of skill in the art typically engage in such experimentation, (4) the nature of the invention is less speculative because (5) the state of the prior art is more developed, (6) the relative skill of those in the art is high, (7) the predictability of the art in this case is established by the large body of literature and years of experience on molecular biology and (8) the breadth of the claims as amended is relatively narrow, limited as it is to C140 receptor polypeptides encoded by nucleic acids having particular characteristics, or C140 receptor polypeptides having percent identity with the identified C140 receptor polypeptide sequences.

While the C140 receptor peptides and nucleic acids described and claimed are novel and unobvious, there is a well-established body of literature regarding the use of prior art hybridization techniques, and peptide sequencing. As noted above, hybridization and peptide sequencing has been used in molecular biology for years. The conditions for hybridization and performing experiments is routine for one skilled in the art, and thus, the claims are properly enabled. Applicants respectfully request the rejection be withdrawn.

III. 35 USC § 112, first paragraph rejections - Written Description

Claims 27, 28, 44, 45, 50, 51, 53-56, 66 and 67 are rejected under 35 USC § 112, first paragraph as failing to comply with the written description requirement. Applicants respectfully traverse the rejection, and requests that it be withdrawn.

Claims 27, 28, 44, 45, 50, and 51 are rejected because the application fails to disclose *any* isolated polypeptides having at least 15 consecutive amino acids being encoded by a nucleotide sequence capable of hybridizing under specifically claimed stringent conditions, or *any* polypeptides having at least 75%, 90% or 95% amino acid sequence identity to either SEQ ID NOs 4 or 63. Applicants respectfully traverse the rejection, however, have amended claims 27 and 44 to expedite prosecution. Applicants agree with the Examiner that the application as originally filed, provides support for isolated C140 receptor polypeptides having at least 15 consecutive amino acid residues, and for C140 receptor polypeptides having at least 75%, 90% or 95% amino acid sequence identity the C140 receptor sequence; thus, claims 27 (from which claims 28, 50 and 51 depend from) and claim 44 (from which claim 45 depends from) have been amended to recite a "C140 receptor" polypeptide. Applicants respectfully request that the rejection be withdrawn in view of these amendments.

Claims 53 - 56, 66 and 67 are rejected under 35 USC § 112, first paragraph for failing to comply with the written description requirement. Specifically, the claimed polypeptide fragments encoded by the specific nucleotides are not supported by the specification, and therefore, is considered new matter. Applicants respectfully traverse this rejection; however, in an effort to expedite prosecution, claims 53 - 56, 66, and 67 have been cancelled. Applicants respectfully request the rejection to be withdrawn because the issue is moot.

Claims 52 and 59 - 69 are rejected under 35 USC § 112, first paragraph for failing to comply with the written description requirement. Specifically, the claims are directed to a genus of isolated polypeptide sequences, and the Examiner asserts that the Applicants are not in possession of a representative number of species to be entitled to claim a genus. Applicants respectfully traverse the rejection, however, have amended claims 27 (from which claims 52, 59 - 62 depend) and 63 (from which claims 64 - 65 and 68 - 69 depend), and cancelled claims 66 and 67 in an effort to facilitate prosecution. This amendment is not to be construed that the Applicants have surrendered subject matter directed to claims related to a genus; rather, the Applicants reserve the right to pursue claims to in continuation applications to subject matter which may no longer be encompassed in the amended claims.

Claims 52, and 59 - 62 all depend upon and include the limitations of claim 27, which has been amended to recite an "isolated C140 receptor polypeptide". Claim 63 (and claims 64, 65, 68 and 69 which depend from it) has also been amended to limit the polypeptides to a "C140 receptor" polypeptide. Thus the polypeptides of claims 52, 59 - 65, 68 and 69 have become limited to a particular species of C140 receptor polypeptides. As the Examiner has pointed out, the Applicants have adequately identified the scope of the C140 receptor polypeptide, and the Applicants respectfully request the rejection be withdrawn.

IV. 35 USC § 112, second paragraph rejection

Claim 48 has been rejected under 35 USC § 112, second paragraph, as being indefinite, because the recitation ". . . comprises amino acid sequences of SEQ ID NO:63" (emphasis added) is unclear. Applicants thank the Examiner for identifying this typographical error, and has amended claim 46 to recite "sequence" as singular. Applicants respectfully request that the rejection be withdrawn, and, as there are no outstanding rejection, claim 48 be allowed.

In this response, Applicants have made a *bona fide* attempt to address all matters raised by the Examiner. Should the Examiner find that this response does not address all matters, Applicants respectfully request the Examiner advise the Applicants of such deficiencies prior to the issuance of the next office communication so that the Applicants may cure such deficiency.

Applicants respectfully submit that the application is now in condition for allowance, and therefore respectfully request that the outstanding rejections be withdrawn and that a Notice of Allowance be issued. If any remaining matters need to be resolved, Applicants respectfully request an interview with the Examiner prior to any official action being taken by the Office in response to these arguments and amendments in order to facilitate allowance of the pending claims. Applicants' undersigned attorney may be contacted at the telephone number set forth below.

Submitted concurrently with this Office Action Response is a Petition for an Extension of Time to respond to the Office Action, including authorization to charge requisite fees to Deposit Account 50-3464. It is believed no other fee or requests for extension of time is required. If

additional fees or requests for extension of time is required, please charge the same to Deposit Account 50-3464.

Respectfully submitted,

Date: October 2, 2006

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